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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,436	12/22/2004	Hilde Azjin	TIP0015 US	7541

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PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,436	AZJIN ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *1,3,4 and 6-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The petition filed under 37 C.F.R. §1.137(b), on 20 December 2006, to revive the application is granted. This Office Action is in response to the amendment filed on 20 December 2006. Claims 1-10 are pending. Claims 1, 3, 4 and 6-10 are withdrawn. Claims 2 and 5 are under final rejection.

Objections

The objection to the title and abstract is **withdrawn** in view of Applicants' amendment.

The objection to claim 2 is **withdrawn** in view of the Applicants' amendment.

Claim Rejections - 35 U.S.C. §112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 2 and 5 under 35 U.S.C. §112, second paragraph, as being indefinite is **maintained**.

Claim 2 recites the limitation "said mutated HIV reverse transcriptase inhibitor" in step (iii). There is insufficient antecedent basis for this limitation in the claim.

In both claims 2 and 5, Applicants' amendment adds the essential method steps in a non-operative order, *i.e.* one skilled in the art cannot perform (iii) correlating a mutation to a change in an HIV drug susceptibility before carrying out the steps (iv) and (v). The recitation of "mutation 194G" is indefinite because it is unclear which genome is used for reference of position 194 and which wild type amino acid residue is changed to G. The phrase "mutated reverse transcriptase inhibitor" is indefinite since the specification does not provide a definition. How is the "mutated reverse transcriptase inhibitor" distinct from a reverse transcriptase inhibitor?

New Matter Rejection

Claims 2 and 5 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The term "a mutated HIV reverse transcriptase inhibitor" or "a mutated RT inhibitor" as recited in claims 2 and 5 is not supported by the original disclosure or claims as filed. The specification does <u>not</u> provide sufficient support for a "mutated" RT inhibitor. The specification and original claims only describe an RT inhibitor, which is taught in the prior art. The instant claims now recite limitations that were not clearly disclosed in the specification as filed, and now change the scope of the instant

disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. §112.

Applicants are required to cancel the new matter in response to this Office Action. Alternatively, Applicants are invited to provide sufficient written support for the new limitations indicated above. See MPEP §714.02, §2163.05-06 and §2173.05 (i).

The rejection of claim 2 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **withdrawn** in view of the amendment.

The rejection of claim 5 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **maintained**.

Examiner's rejection in the Action mailed on 13 March 2006 is as follows:

Claims 2 and 5 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for evaluating the effectiveness of a reverse transcriptase inhibitor for HIV strains with a mutation at position 194 in the reverse transcriptase region, does not reasonably provide enablement for determining the susceptibility or effectiveness of other HIV drugs and other viral drugs in viral strains containing drug-resistant mutations at positions other than 194. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (BdPatApplnt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The nature of the instant invention is a method for evaluating the effectiveness of a reverse transcriptase inhibitor as an antiviral therapy for a patient infected with at least one mutant HIV strain, or for evaluating a change in the viral drug susceptibility, comprising: (i) collecting a sample from an HIV-infected patient; (ii) determining whether the sample comprises a nucleic acid encoding HIV reverse transcriptase having at least one mutation 194G; (iii) correlating the presence of said at least one mutation of step (ii) to a change in effectiveness of said reverse transcriptase inhibitor or in viral drug susceptibility. The breadth of the instant claims is so broad that it encompasses all anti-viral drugs.

The guidance presented in the specification is limited to the detection of drug-resistant mutations at positions 194 in HIV reverse transcriptase. The specification does not provide the drug-resistance mutation profile for any viruses other than HIV. One skilled in the art cannot use the instant invention for other viral drugs because the mutation at position 194 is specific for HIV reverse transcriptase but not other HIV enzymes or other viruses.

It is well known in the art that HIV is highly evolutionary and develops a wide spectrum of escape mutants (Shafer, 1999) towards not only reverse transcriptase inhibitors but also drugs acting at different sites in an HIV particle, such as protease inhibitors and fusion inhibitors. Due to this unpredictable nature, one skilled in the art would not be able to assess the susceptibility for all HIV drugs using only the single point mutation provided in the instant claims and specification.

Applicants' amendment changed the scope of the invention from evaluating a viral drug to evaluating an HIV drug. However, as indicated in the previous Action, the specification is not enabling for other HIV drugs than reverse transcriptase inhibitors. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 2 and 5 under 35 U.S.C. §103(a) as being obvious over Stein *et al.* (1994) in view of Servais *et al.* (1994) is **maintained** for reasons of record.

Examiner's rejection in the Action mailed on 13 March 2006 is as follows:

Stein *et al.* disclose sequence analysis of HIV RT from HIV patients comprising collecting a sample from an HIV-infected patient; determining whether the sample comprises a nucleic acid encoding HIV reverse transcriptase having at least one mutation at position 194; and correlating the presence of the mutations to a change in effectiveness or susceptibility of AZT, a reverse transcriptase inhibitor.

Stein *et al.* do not disclose the specific amino acid change to G at position 194. However, Servais *et al.* disclose that the 194G mutation is found in the patient isolates in an assay for HIV-1 drug resistance mutations.

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to combine the drug-resistance mutation profiles taught by Stein *et al.* and Servais *et al.* such that the modified method has a more comprehensive mutation profile. One having ordinary skill in the art would have been motivated to do this so that the new mutation profile contributes to a more complete and accurate drug evaluation. Thus, claims 2 and 5 are obvious over Stein *et al.* in view of Servais *et al.*

Applicants assert that the prior art do not teach a method of evaluating a drug that inhibits the RT having a mutation at 194. Applicants further assert that the amended claims are drawn to an invention that is distinguished from the prior art because of the new limitation "mutated RT inhibitor" in the amended claims.

Applicants' arguments have been fully considered but are not persuasive. Applicants argue that Stein *et al.* clearly teach that AZT is NOT an inhibitor to the mutated RT since the HIV having RT mutations at position 194 were isolated from the AZT-resistant HIV patients. However, an inhibitor to the mutated RT is NOT the

claimed invention. The instant invention is a method for evaluating whether an HIV RT inhibitor is effective as a therapy for the infection of at least one mutant HIV strain. Each method step is taught or suggested in Stein *et al.* and Servais *et al.* combined together. Step (i) -collecting a sample from an HIV-infected patient - is taught in Stein *et al.* See Abstract and page 116, Materials and Methods. Step (ii) is taught in stein et al. See page 117-118, Nucleotide Sequence Analysis of RT, where Stein *et al.* suggest determining amino acid substitutions in various positions including 194. Servais *et al.* specifically suggest the mutation 194G that is correlated with resistance to HIV therapy. See the published amino acid sequence of the mutant HIV strain, as attached in the last Office Action mailed on 13 March 2006. Therefore, all method steps have been described in the cited prior art. Applicants also argue that Servais *et al.* only disclose an RT with mutation 194G from patients failing anti HIV therapy. It is not recited anywhere in the claims that a patient in the claimed method cannot be failing one anti-HIV therapy.

In response to Applicants' In response to applicant's argument that Stein *et al.* and Servais *et al.* do not teach nor suggest the evaluation of a mutated RT inhibitor, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Since Applicants did not clearly point out the difference in the method steps between the invention and the method taught by Stein *et al.* and Servais *et al.*, the cited art meet the claims.

Conclusion

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
28 February 2007

Louise Humphrey, Ph.D.
Assistant Examiner